ature for 5.5 h. The mixture was poured into an ice-$Na_2S_2O_3$ solution, extracted with ether, dried ($MgSO_4$), filtered, and evaporated to leave a crude oil. It was purified by 0.5-mm SiO_2 plates to give 68 mg (83%) of **28** as a yellow oil: IR ($CHCl_3$) 1715, 1675, 1600, 1165, 905 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.53 (s, 3 H), 7.25-7.70 (m, 3 H), 7.86-8.23 (m, 2 H). Spectral data were identical with those of an authentic specimen.[19]

(19) Hartman, W. W.; Roll, L. J. "Organic Syntheses"; Wiley: New York, 1965; Collect. Vol. 3, p 20.
(20) The group notation is being changed in accord with recent actions by IUPAC and ACS nomenclature committees. A and B notation is being eliminated because of wide confusion. Group I becomes groups 1 and 11, group II becomes groups 2 and 12, group III becomes groups 3 and 13, etc.

Registry No. **1a**, 79143-99-0; **1b**, 86137-19-1; **1c**, 79144-08-4; **1d**, 94620-84-5; **1e**, 94620-85-6; **1f**, 94620-86-7; **1g**, 94620-87-8; **1h**, 94620-88-9; (*R**,*R**)-**1i**, 94620-89-0; (*R**,*S**)-**1i**, 94620-90-3; (*R**,*R**)-**1j**, 94620-91-4; (*R**,*S**)-**1j**, 94620-92-5; **1k**, 94620-93-6; **2a**, 79144-00-6; **2c**, 79144-09-5; **3**, 79144-01-7; **4**, 79144-02-8; **5a**, 64554-58-1; **5b**, 79144-10-8; (*R**,*R**)-**5c**, 94620-81-2; (*R**,*S**)-**5c**, 94620-99-2; **6a**, 79144-05-1; **10a**, 94620-82-3; **10c**, 94620-83-4; **11a**, 94620-94-7; **11b**, 94620-96-9; **12**, 94620-95-8; **17**, 86137-20-4; **18**, 86137-22-6; **19**, 86137-21-5; **26**, 94620-97-0; **27**, 94620-98-1; **28**, 579-07-7; *sec*-BuLi, 598-30-1; MeI, 74-88-4; EtI, 75-03-6; *i*-PrI, 75-30-9; *i*-BuI, 513-38-2; $(MeS)_2$, 624-92-0; PhCHO, 100-52-7; PhCH=CHCHO, 104-55-2; PhCOPh, 119-61-9; $ClP(S)Me_2$, 993-12-4; PhCN, 100-47-0; C_2H_5SH, 75-08-1; $C_2H_5OCH_2Cl$, 3188-13-4; $C_2H_5SCH_2OC_2H_5$, 54699-20-6; $PhCOCO_2H$, 611-73-4; $CH_3S(CH_2)_3OH$, 505-10-2; cyclohexanone, 108-94-1.

Polyaza Cavity Shaped Molecules. 2. Annelated Derivatives of 2,2'-Biquinoline and the Corresponding *N*-Oxides

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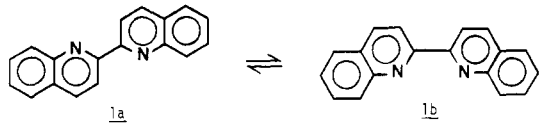
The reaction of *o*-aminobenzaldehyde with cyclic 1,2-diketones provided 3,3'-annelated derivatives of 2,2'-biquinoline. The reaction with 1,2-cyclododecanedione stopped at the monocondensation stage. High-resolution NMR spectra demonstrate that the dimethylene- and trimethylene-bridged systems are undergoing rapid conformational inversion at room temperature while the tetramethylene-bridged system is conformationally rigid. The chemical shift of the H-8 proton is found to be closely related to the biquinoline dihedral angle. Mono- and di-*N*-oxides were prepared by reaction of annelated biquinolines with *m*-chloroperbenzoic acid. The di-*N*-oxide of the trimethylene-bridged system was found to be conformationally rigid by NMR.

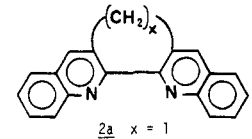
The 2,2'-biquinoline molecule can be considered as a dibenzo derivative of 2,2'-bipyridine. It may exist in two planar conformations: anti (**1a**) and syn (**1b**). An X-ray



1a **1b**

determination has revealed that the anti form is preferred in the solid state.[1] It is the syn form, however, through which bidentate chelation can occur. As has been pointed out by earlier workers,[2,3] the fused benzo rings serve to sterically congest the coordinating pocket of the molecule in its syn conformation and limit the types of complexation which can occur.

We have prepared a series of 3,3'-annelated 2,2'-biquinolines **2** in which the length of the annelating bridge controls the relative orientation of the two rings and thus influences the shape of the chelating "bite" as well as other types of cooperative chemistry which the two nitrogens might undergo. In this paper we discuss the preparation of the annelated biquinolines **2a-d**, a spectroscopic investigation of their conformational properties, and the preparation and characterization of mono- and di-*N*-oxide derivatives.



2a x = 1
b x = 2
c x = 3
d x = 4

Synthesis. The reaction of *o*-acetyl- or *o*-benzoylaniline with cyclic α-diketones has been utilized to prepare 4,4'-disubstituted derivatives of **2a-c**.[4] It has also been demonstrated that *o*-aminobenzaldehyde will condense with 1,2-cyclohexanedione to provide **2b**.[5] We have applied this same reaction to a series of cyclic α-diketones ranging from 5 to 12 carbons in ring size. For rings up to eight carbons, the condensation occurs smoothly to provide **2a-d** in good yields. Previously we have reported that this same type of condensation may be carried out with 2-aminonicotinaldehyde to provide 3,3'-annelated 2,2'-bi[1,8]-naphthyridines.[6] The reaction of *o*-aminobenzaldehyde with 1,2-cyclododecanedione occurs at only one carbonyl group such that the monocondensation product **5** is formed exclusively. In an independent study we are investigating

(1) Folting, K.; Merritt, L. L., Jr. *Acta Crystallogr.* **1977**, *B33*, 3540.
(2) Klassen, D. M. *Inorg. Chem.* **1976**, *15*, 3166.
(3) Harris, C. M.; Patil, H. R. H.; Sinn, E. *Inorg. Chem.* **1967**, *6*, 1102.
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(5) Uhlemann, E.; Thomas, Ph.; Kempter, G. *Z. Anorg. Allg. Chem.* **1965**, *341*, 11.
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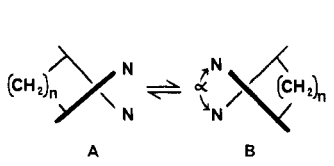


n	α	Estimated Barrier
1	0°	0 Kcal/mole
2	20	≤4
3	50	≤13
4	65	
8	≤180	

Figure 1.

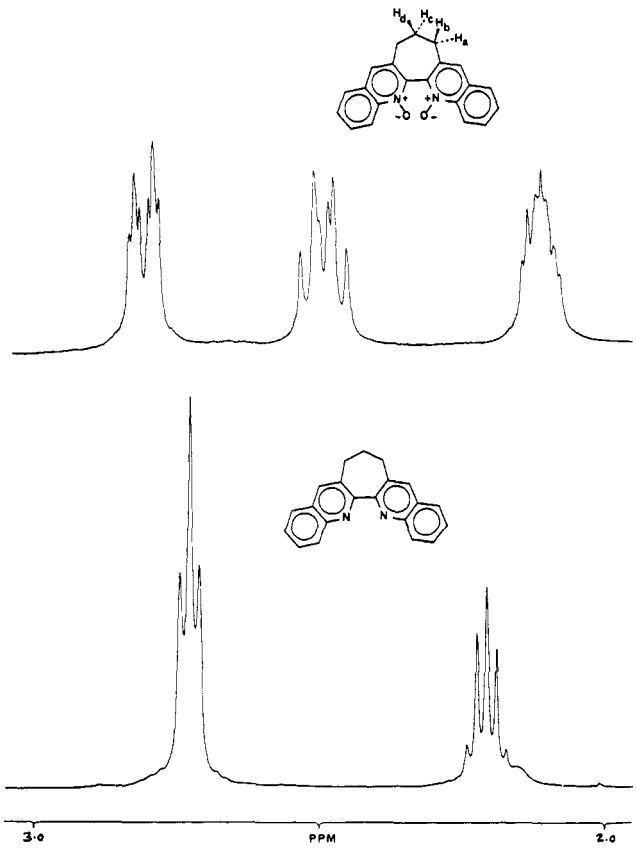
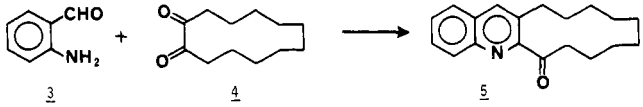


Figure 2. 400-MHz ^{1}H NMR spectrum of the upfield region of di-*N*-oxide **9b** vs. parent biquinoline **2c**.

the effect of nitrogen lone pair orientation on adjacent carbonyl group reactivity to explain the relative reactivity of pyridyl ketones such as **5**.



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Properties. The most significant structural feature of the biquinolines **2** is the variation of the dihedral angle α as a function of the length of the annelating bridge. A careful examination of molecular models allows one to estimate values of α, and these are in good accord with earlier estimates summarized by Calder et al.[7] and shown in Figure 1. For the bridged biphenyl systems (n = 2, 3), Mislow has calculated inversion barriers[8] which should represent upper limits for the corresponding bipyridines or biquinolines since the steric interaction of two nitrogen lone pairs has been shown to be less than that for two benzene C–H bond in studies on [2.2]metacyclophane and its pyridine analogue.[9] If the barrier to inversion is sufficiently high at room temperature it should be possible

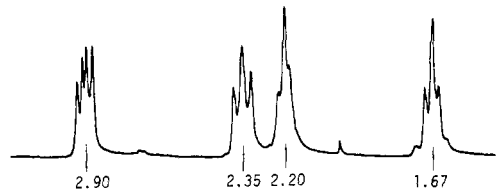


Figure 3. Upfield region of 400-MHz ^{1}H NMR of **2d** at 25 °C.

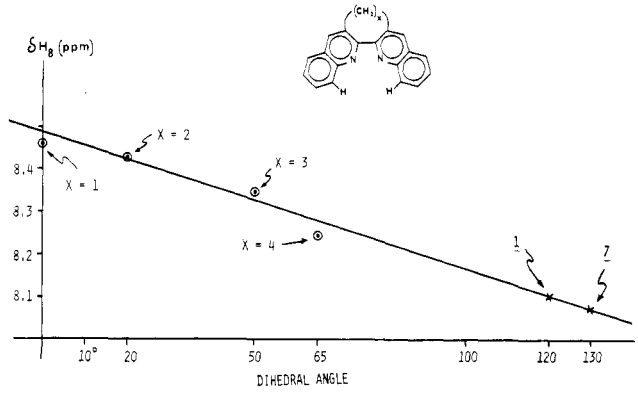
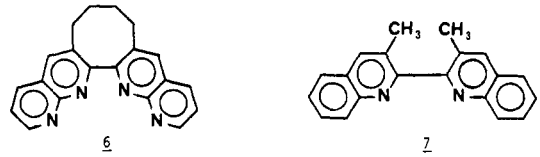


Figure 4. Relationship between H-8 chemical shift of annelated 2,2′-biquinolines and dihedral angle.

to separate the enantiomers A and B.

The room-temperature NMR spectra of **2a** and **2b** show singlets for the bridge protons at 4.20 and 3.20 ppm, respectively. The trimethylene bridge of **2c** shows a triplet at 2.7 ppm and a quintet at 2.2 ppm, indicating rapid conformational inversion of the molecule (Figure 2). At 400 MHz the tetramethylene bridge of **2d** may be observed as four distinct signals (Figure 3). The well resolved nature of the $(AA',BB')_2$ system may be understood after careful examination of a molecular model. One of the α-methylene protons lies nearly in the plane of the adjacent aromatic ring and is thus substantially deshielded, resonating at 2.90 ppm. On the other hand, the other α-methylene proton is oriented toward the shielding region of the nonadjacent quinoline ring and thus absorbs at higher field, 2.35 ppm.

By slowly heating a sample of **2d** dissolved in *o*-xylene-d_{10} up to 135 °C and recording the 400-MHz ^{1}H NMR spectra as a function of temperature, we were able to observe substantial broadening of all four upfield signals as well as some coalescence of the signals at 2.90 and 2.35 ppm and those at 2.20 and 1.67 ppm. Calculation of an approximate ΔG value for the conformational inversion process (A $\rightleftarrows$ B, Figure 1) by analysis of the line broadening is complicated by the fact that the coalescing signals are coupled to one another as well as to the adjacent methylene protons.[10] A variable-temperature NMR study was also carried out for the closely related 3,3′-tetramethylene-2,2′-bi-1,8-naphthyridine (**6**), and spectra very



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similar to those for **2d** were obtained. We expect the inversion barriers for these two molecules to be comparable, but an accurate estimate of this value will require the analysis of a less coupled system.

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(8) Mislow, K.; Glass, M. A. W.; Hopps, H. B.; Simon, E.; Wahl, G. H., Jr. *J. Am. Chem. Soc.* **1964**, *86*, 1710.
(9) Gault, I.; Price, B. J.; Sutherland, I. O. *Chem. Commun.* **1967**, 540.
(10) Allerhand, A.; Gutowsky, H. S.; Jonas, J.; Meinzer, R. A. *J. Am. Chem. Soc.* **1966**, *88*, 3185.

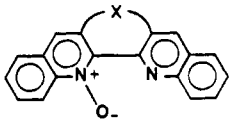
Table I. Ultraviolet Absorption Data for 2,2′-Biquinolines

biquinoline	λ_{max} (95% EtOH), nm (ϵ)	
1	257 (71 500)	315 (19 500)
		325 (22 000)
		335 (18 000)
7	237 (69 500)	307 (9500)
		312 (9000)
		320 (12 500)
2a	252 (55 000)	340 (24 000)
	258 (60 000)	350 (21 000)
		360 (49 000)
2b	262 (81 000)	344 (23 000)
		360 (27 000)
2c	255 (70 000)	320 (15 000)
		330 (15 000)
2d	235 (54 000)	310 (13 000)
	245 (53 000)	325 (12 000)

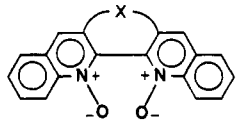
An interesting observation on the solution conformation of unbridged 2,2′-biquinolines may be made by examination of the H-8 resonance. The chemical shift of this proton is sensitive to the dihedral angle (α) between the two quinoline rings. As this angle becomes close to zero, the H-8 proton becomes more deshielded and resonates at a lower field. If the approximate values of α given in Figure 1 are plotted against the H-8 chemical shift for **2a–d**, a nearly straight line is obtained (Figure 4). Extrapolation of this line to the H-8 values observed for 2,2′-biquinoline (1) and its 3,3′-dimethyl derivative **7** allows one to estimate α values of 130° and 120° respectively for these two systems. It is not surprising that the more sterically hindered 3,3′-dimethyl compound should be less planar than the unsubstituted parent system.

The correlation between UV absorptions and dihedral angle is also good. Table I summarizes the absorption maxima and extinction coefficients for **2a–d** as well as 2,2′-biquinoline and its dimethyl derivative. The long wavelength band of **2a** shows the well-resolved fine structure which would be expected from such a rigid, planar molecule. As the 3,3′-bridge is increased from two to four carbons, there is a shift to higher energy, less intense absorptions. This observation is explained by the concurrent decrease in the conjugative interaction between the two quinoline rings.

***N*-Oxide Derivatives.** Recently Wenkert and Woodward have reported on the di-*N*-oxide of 2,2′-bipyridine as a potential source of singlet oxygen.[11] The parent system as well as a variety of 4,4′-disubstituted derivatives were examined in refluxing solvents and under sublimation conditions but no singlet oxygen evolution was observed. Apparently these molecules vastly prefer a transoid geometry which is unfavorable toward interaction of the two *N*-oxide moieties. The opposite extreme is found in the 1,10-phenanthroline system which at first was incorrectly reported to form a di-*N*-oxide.[12] Corey and co-workers subsequently demonstrated that for steric reasons only a mono-*N*-oxide can be formed.[13] It became of interest to us to determine under what conditions *N*-oxides of the annelated biquinolines **2a–d** could be formed. The parent system, 2,2′-biquinoline, upon treatment with 2.5 equiv of oxidizing agent, forms either mono- or di-*N*-oxide, depending on the reaction time employed. Treatment of the dimethylene bridged **2b** with excess *m*-chloroperbenzoic acid (*m*-CPBA) leads only to mono-*N*-oxide. On the other hand, the tetramethylene bridged **2d** gives mono-*N*-oxide **8c** with 1 equiv of *m*-CPBA and di-*N*-oxide **9c** with excess



8a X = H,H
b X = $-CH_2CH_2-$
c X = $-(CH_2)_4-$



9a X = H,H
b X = $-(CH_2)_3-$
c X = $-(CH_2)_4-$

reagent. Interestingly, the trimethylene-bridged system **2c** appears reluctant to stop at the mono-*N*-oxide stage but does readily form the di-*N*-oxide **9b**. Compounds **8** and **9** may be easily distinguished by the symmetry of their ^1H NMR spectra, the former systems showing twice as many aromatic signals as the latter.

The two *N*-oxide moieties of **9b** and **9c** are held within reasonable proximity to one another such that the geometric problems encountered by Wenkert and Woodward relating to singlet oxygen generation might be overcome. We examined the viability of these systems as singlet oxygen precursors by heating their toluene solutions in the presence of 1,3-diphenylisobenzofuran, an efficient singlet oxygen trap.[14] After 12 h at 160 °C in a sealed tube under nitrogen, nearly all of the unreacted di-*N*-oxide **9b** was recovered as was the diphenylisobenzofuran. There was no evidence for the formation of **2c** and only a trace amount of *o*-dibenzoylbenzene was observed. These results are less surprising in light of an orbital symmetry treatment of this reaction. Any pathway which conserves a mirror plane of symmetry bisecting the di-*N*-oxide reactant and the $^1O_2$–diazine products is rigorously "symmetry forbidden" and would have an extraordinarily high activation energy. A path which conserves a C_2 axis is symmetry allowed; however, geometric and electronic considerations make it highly unlikely.

Di-*N*-oxide formation has an interesting stereochemical consequence for the trimethylene-bridged biquinoline **2c**. The incorporation of two oxygens in the "pocket" of the molecule provides sufficient congestion to hinder conformational inversion (Figure 2). Thus the protons H_a and H_b become magnetically nonequivalent and the triplet observed at 2.7 ppm for **2c** splits into two doublets of triplets for **9b** centered at 2.80 and 2.47 ppm with a geminal coupling constant of 13.8 Hz.

With a good understanding of the conformational properties of annelated 2,2′-biquinolines and their corresponding *N*-oxides, we are now embarking on a careful study of their coordination with various metals.

Experimental Section

Nuclear magnetic resonance spectra were obtained on a Varian Associates T-60 or FT-80 or a Nicolet NT-300 WB or a Bruker WH-400 spectrometer (University of South Carolina Magnetic Resonance Laboratory) and chemical shifts are reported in parts per million downfield from Me_4Si. Infrared spectra were obtained on a Beckman IR-4250 spectrometer. Ultraviolet spectra were obtained on a Cary 14 spectrometer. Mass spectra were obtained by direct sample introduction into a Hewlett-Packard 5933A GC–mass spectrometer. All solvents were freshly distilled reagent grade. 2-Aminobenzaldehyde was prepared according to a literature procedure.[15] All melting points are uncorrected.

3,3′-Methylene-2,2′-biquinoline (2a). To a solution of 0.5 g (4.1 mmol) of 2-aminobenzaldehyde and 0.19 g (2.0 mmol) of 1,2-cyclopentanedione[16] in 25 mL of absolute ethanol was added 0.04 g of KOH dissolved in 2 mL of absolute ethanol. The solution

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(16) Acheson, R. M. *J. Chem. Soc.* **1956**, 4232.

was refluxed under nitrogen for 4 h. Unreacted starting materials were recovered by chromatography on 40 g of silica gel, eluting with dichloromethane. Further elution with ethyl acetate afforded 0.25 g (47%) of **2a** which was recrystallized from ethyl acetate to afford a yellow solid: mp 281–283 °C; ^{1}H NMR (400 MHz, $CDCl_3$) 8.46 (d of d, H_8 and $H_{8'}$, $J_{7,8}$ = 8.55, $J_{6,8}$ = 1.06 Hz), 2.26 (s, H_4 and $H_{4'}$), 7.82 (d of d, H_5 and $H_{5'}$, $J_{5,6}$ = 8.13, $J_{5,7}$ = 1.29 Hz), 7.74 (t of d, H_7 and $H_{7'}$, $J_{6,7}$ = 6.98 Hz), 7.55 (t of d, H_6 and $H_{6'}$), and 4.20 (s, -CH_2-); IR (KBr) 1630, 1570, 1500, 1425, 1405, 1245, 1195, 1155, 1135, 1105, 1030, 970, 940, 905, 865, 790, and 760 cm^{-1}; UV max (95% C_2H_5OH) 252 (ϵ 55 000), 258 (60 000), 340 (24 000), 350 (21 000), and 360 nm (49 000); mass spectrum, *m/e* (relative intensity) 268 (100, parent ion); exact mass calcd for $C_{19}H_{12}N_2$ *m/e* 268.10004, found 268.0994.

3,3′-Dimethylene-2,2′-biquinoline (2b). The same procedure described above for **2a** was followed, using 0.8 g (6.6 mmol) of 2-aminobenzaldehyde and 0.4 g (3.3 mmol) of 1,2-cyclohexanedione,[17] to give 0.76 g (72%) of **2b** which was recrystallized from ethyl acetate to afford white crystals: mp 185 °C (lit.[5] mp 190 °C); ^{1}H NMR (400 MHz, $CDCl_3$) 8.43 (d, H_8 and $H_{8'}$, $J_{7,8}$ = 8.48 Hz), 8.03 (s, H_4 and $H_{4'}$), 7.77 (d, H_5 and $H_{5'}$, $J_{5,6}$ = 8.05 Hz), 7.68 (t, H_7 and $H_{7'}$, $J_{6,7}$ = 7.00 Hz), 7.52 (t, H_6 and $H_{6'}$), and 3.2 (s, 4 H, -CH_2-); IR (KBr) 1610, 1500, 1445, 1420, 1390, 1350, 1250, 1220, 1150, 1105, 1040, 910, 800, 760 cm^{-1}; UV max (95% C_2H_5OH) 262 (ϵ 81 000), 344 (23 000), and 360 nm (27 000); mass spectrum, *m/e* (relative intensity) 283 (22), 282 (100, parent ion), 281 (54), and 279 (11).

3,3′-Trimethylene-2,2′-biquinoline (2c). The same procedure described above for **2a** was followed, using 0.8 g (6.6 mmol) of 2-aminobenzaldehyde and 0.42 g (3.3 mmol) of 1,2-cycloheptanedione,[18] to give 0.35 g (36%) of **2c** which was recrystallized from ethyl acetate–hexane to afford pale yellow needles: mp 203–204 °C; ^{1}H NMR (400 MHz, $CDCl_3$) 8.35 (d, H_8 and $H_{8'}$, $J_{7,8}$ = 8.47 Hz); 8.00 (s, H_4 and $H_{4'}$), 7.81 (d, H_5 and $H_{5'}$, $J_{5,6}$ = 8.11 Hz), 7.69 (t, H_7 and $H_{7'}$, $J_{6,7}$ = 7.01 Hz), 7.54 (t, H_6 and $H_{6'}$) 2.7 (t, 4 H, α-CH_2-), and 2.2 (quintet, 2 H, β-CH_2-); IR (KBr) 1605, 1490, 1445, 1410, 1160, 1000, 750 cm^{-1}; UV max (95% C_2H_5OH) 255 (ϵ 70 000), 320 (15 000), and 330 nm (15 000); mass spectrum *m/e* (relative intensity) 296 (100, parent ion), 295 (62), 268 (28), and 297 (24); exact mass calcd for $C_{21}H_{16}N_2$ *m/e* 296.13134, found 296.1306.

3,3′-Tetramethylene-2,2′-biquinoline (2d). The same procedure described above for **2a** was followed, using 0.8 g (6.6 mmol) of 2-aminobenzaldehyde and 0.48 g (3.3 mmol) of 1,2-cyclooctanedione,[19] to give 0.72 g (70%) of **2d** which was recrystallized from ethyl acetate to afford colorless crystals: mp 236–237 °C; ^{1}H NMR (400 MHz, $CDCl_3$) 8.25 (d, H_8 and $H_{8'}$, J = 8.43 Hz), 8.04 (s, H_4 and $H_{4'}$), 7.80 (d, H_5 and $H_{5'}$, $J_{5,6}$ = 8.05 Hz), 7.66 (t, H_7 and $H_{7'}$, $J_{6,7}$ = 6.97 Hz), 7.52 (t, H_6 and $H_{6'}$), 2.90 (q, 2 H), 2.35 (t, 2 H), 2.2 (t, 2 H), 1.67 (quintet, 2 H); IR (KBr) 2910, 1595, 1482, 1405, 1125, 1095, 1025, 890, 857, 834, 780, and 745 cm^{-1}; UV max (95% C_2H_5OH) 235 (ϵ 54 000), 245 (53 000), 310 (13 000), 325 nm (12 000); mass spectrum, *m/e* (relative intensity) 310 (43, parent ion), 281 (100) and 140 (23); exact mass calcd for $C_{22}H_{18}N_2$ *m/e* 310.14699, found 310.1469.

3,3′-Dimethyl-2,2′-biquinoline (7). The same procedure described above for **2a** was followed, using 0.43 g (3.5 mmol) of 2-aminobenzaldehyde and 0.21 g (1.8 mmol) of 3,4-hexanedione,[20] to give 0.4 g (83%) of **7** which was recrystallized from ethyl acetate–hexane to afford colorless needles: mp 143–144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) 8.11 (d, H_8 and $H_{8'}$, $J_{7,8}$ = 8.39 Hz), 8.07 (s, H_4 and $H_{4'}$), 7.80 (d, H_5 and $H_{5'}$, $J_{5,6}$ = 8.11 Hz), 7.65 (t, H_7 and $H_{7'}$, $J_{6,7}$ = 7.23 Hz), 7.52 (H_6 and $H_{6'}$, t), and 2.3 (s, 6 H, CH_3); IR (KBr) 1595, 1485, 1440, 1130, 1100, 1020, 995, 900, and 745 cm^{-1}; UV max (95% C_2H_5OH) 237 (ϵ 69 500), 307 (9500), 312 (9000), and 320 nm (12 500); mass spectrum, *m/e* (relative intensity) 284 (63, parent ion), 269 (100).

2,2′-Biquinoline *N*-Oxide (8a). To a stirred solution of 0.5 g (1.95 mmol) of 2,2′-biquinoline in 30 mL of dichloromethane at 2 °C was slowly added a solution of 0.84 g (4.87 mmol) of *m*-chloroperbenzoic acid in 10 mL of dichloromethane. The resulting yellow solution was stirred at room temperature for 2 h and then diluted with 100 mL of dichloromethane, washed with 5% sodium carbonate (2 × 100 mL), and dried over anhydrous magnesium sulfate. After filtration and removal of solvent, the residue was chromatographed on silica gel, eluting with dichloromethane followed by dichloromethane–ethyl acetate to afford 0.3 g (53%) of the mono-*N*-oxide **8a** which was recrystallized from methanol to afford cream colored crystals: mp 170–172 °C; ^{1}H NMR (400 MHz, $CDCl_3$) 8.92 (d, H_3, $J_{3,4}$ = 8.7 Hz), 8.86 (d, $H_{8'}$, $J_{7',8'}$ = 8.8 Hz), 8.28 (d, $H_{3'}$, $J_{3',4'}$ = 8.5 Hz), 8.27 (d, H_8, $J_{7,8}$ = 8.8 Hz), 8.18 (d, H_4), 7.87 (br d, H_5 and $H_{5'}$), 7.81 (d, $H_{4'}$), 7.78 (t of d, $H_{7'}$, $J_{6',7'}$ = 7.9, $J_{5',7'}$ = 1.36 Hz), 7.73 (t of d, H_7, $J_{6,7}$ = 7.7, $J_{5,7}$ = 1.41 Hz), 7.65 (t of d, $H_{6'}$, $J_{6',8'}$ = 1.15 Hz), 7.58 (t of d, H_6, $J_{6,8}$ = 1.12 Hz); IR (KBr) 1600, 1560, 1500, 1425, 1370, 1325, 1305, 1255, 1245, 1210, 1150, 1130, 1105, 1070, 910, 880, 840, 810, 770, and 750 cm^{-1}.

3,3′-Dimethylene-2,2′-biquinoline *N*-Oxide (8b). The same procedure described above for **8a** was followed, using 0.14 g (0.5 mmol) of **2b** and 0.08 g (0.5 mmol) of *m*-chloroperbenzoic acid, to afford 0.12 g (81%) of **8b** as a yellow solid which was recrystallized from chloroform: mp 150–152 °C; ^{1}H NMR (400 MHz, $CDCl_3$) 8.87 (d, $H_{8'}$, $J_{7',8'}$ = 8.7 Hz), 8.29 (d, H_8, $J_{7,8}$ = 8.4 Hz), 7.98 (s, H_4), 7.66 (m, H_5, $H_{5'}$, $H_{6'}$, $H_{7'}$), 7.51 (overlapping t, H_6, H_7), 7.47 (s, $H_{4'}$), 2.99 (s, -CH_2-); IR (KBr) 1605, 1570, 1490, 1440, 1345, 1295, 1140, 1100, 900, 775, 750 cm^{-1}.

3,3′-Tetramethylene-2,2′-biquinoline *N*-Oxide (8c). The same procedure described above for **8a** was followed, using 0.10 g (0.32 mmol) of **2d** and 0.055 g (0.32 mmol) of *m*-chloroperbenzoic acid, to afford 0.05 g (48%) of **8c** as a white solid which was recrystallized from chloroform: mp 155–159 °C; ^{1}H NMR (400 MHz, $CDCl_3$) 8.74 (d, $H_{8'}$, $J_{7',8'}$ = 8.7 Hz), 8.20 (d, H_8, $J_{7,8}$ = 8.5 Hz), 8.15 (s, H_4), 7.72–7.53 (m, H_5 and $H_{5'}$, H_6 and $H_{6'}$, H_7 and $H_{7'}$), 7.63 (s, $H_{4'}$), 2.93 (m, 2 H), 2.48 (m, 1 H), 2.20 (m, 2 H), 1.60 (m, 3 H); IR (KBr) 1600, 1565, 1495, 1440, 1335, 1230, 1140, 1045, 775, 750 cm^{-1}.

2,2′-Biquinoline *N*,*N*′-Dioxide (9a). To a stirred solution of 0.25 g (0.97 mmol) of 2,2′-biquinoline in 2 mL of dichloromethane at 25 °C was slowly added a solution of 0.43 g (2.4 mmol) of *m*-chloroperbenzoic acid in 10 mL of dichloromethane. The resulting yellow solution was stirred at room temperature for 72 h and then diluted with 100 mL of dichloromethane, washed with 5% sodium carbonate (2 × 100 mL), and dried over anhydrous magnesium sulfate. After filtration and removal of solvent, the residue was chromatographed on silica gel, eluting with ethyl acetate followed by 50% ethyl acetate–methanol, to afford 0.2 g (72%) of di-*N*-oxide **9a** which was recrystallized from methanol: mp 257–258 °C (lit.[21] mp 257 °C); ^{1}H NMR (400 MHz, $CDCl_3$) 8.81 (d, H_8 and $H_{8'}$, $J_{7,8}$ = 8.8 Hz), 7.88 (d, H_3 and $H_{3'}$, $J_{3,4}$ = 7.9 Hz), 7.8 (m, H_4 and $H_{4'}$, H_5 and $H_{5'}$, H_7 and $H_{7'}$), 7.67 (t, H_6 and $H_{6'}$, J = 7.4 Hz); IR (KBr) 1565, 1375, 1340, 1290, 1210, 1130, 1100, 940, 905, 815, and 750 cm^{-1}.

3,3′-Trimethylene-2,2′-biquinoline *N*,*N*′-Dioxide (9b). The same procedure described above for **9a** was followed, using 0.13 g (0.47 mmol) of **2c** and 0.20 g (1.18 mmol) of *m*-chloroperbenzoic acid to afford 0.12 g (78%) of **9b** which was recrystallized from chloroform: mp 255–257 °C; ^{1}H NMR (400 MHz, $CDCl_3$) 8.82 (d, H_8 and $H_{8'}$, $J_{7,8}$ = 8.7 Hz), 7.78 (d, H_5 and $H_{5'}$, $J_{5,6}$ = 7.8 Hz), 7.66 (t of d, H_7 and $H_{7'}$, $J_{6,7}$ = 7.7, $J_{5,7}$ = 1.05 Hz), 7.58 (t of d, H_6 and $H_{6'}$, $J_{6,8}$ = 1.0 Hz), 7.50 (s, H_4 and $H_{4'}$), 2.80 (d of t, α-CH-, J_{gem} = 13.8, $J_{\alpha,\beta}$ = 3.8 Hz), 2.47 (d of t, α-CH-, $J_{\alpha,\beta}$ = 9.9 Hz), 2.07 (m, 2, β-CH_2-); IR (KBr) 2930, 1565, 1490, 1450, 1330, 1220, 1130, 1090, 880, 770, and 750 cm^{-1}.

3,3′-Tetramethylene-2,2′-biquinoline *N*,*N*′-Dioxide (9c). The same procedure described above for **9a** was followed, using 0.31 g (1 mmol) of **2d** and 0.43 g (2.5 mmol) of *m*-chloroperbenzoic acid, to afford 0.23 g (68%) of **9c** which was recrystallized from ethyl acetate to give pale yellow crystals: mp 285 °C; ^{1}H NMR (400 MHz, $CDCl_3$) 8.76 (d, H_8 and $H_{8'}$, $J_{7,8}$ = 8.4 Hz), 7.78 (d, H_5 and $H_{5'}$, $J_{5,6}$ = 7.9 Hz), 7.64 (m, H_7 and $H_{7'}$), 7.59 (s, H_4 and $H_{4'}$),

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7.55 (m, H_6 and $H_{6'}$), 2.91 (d of d, 2 H), 2.25 (t, 2 H), 2.16 (t, 2 H), 1.57 (quintet, 2 H); IR (KBr) 2940, 1565, 1500, 1455, 1330, 1220, 1140, 1090, 1050, 1020, 970, 940, 880, 840, 780, 750 cm^{-1}.

8,9,10,11,12,13,14,15-Octahydrocyclododeca[*b*]quinolin-6-(7*H*)-one (5). The same procedure described above for **2a** was followed, using 0.5 g (4.1 mmol) of 2-aminobenzaldehyde and 0.4 g (2.0 mmol) of 1,2-cyclododecanedione,[22] to give a crude product which was collected as an oil after chromatography. Kugelrohr distillation afforded 0.2 g (35%) of **5**: bp 210 °C (0.2 mm), mp 56-59 °C; ^1H NMR (80 MHz, $CDCl_3$) 7.7 (m, 5 H), 3.0 (m, 4 H), 1.7 (br m, 14 H); ^{13}C NMR (20 MHz, $CDCl_3$) 162.6, 146.5, 135.7, 128.5, 128.3, 126.7, 125.4, 32.7, 29.7, 28.4, 26.7, 26.4, 26.0, 25.4, 23.13, and 23.07 ppm; IR (KBr) 1670 cm^{-1}; 2,4-DNP mp 188 °C.

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Registry No. 1, 119-91-5; **2a**, 318-55-8; **2b**, 5967-35-1; **2c**, 94537-45-8; **2d**, 94537-46-9; **3**, 529-23-7; **4**, 23427-68-1; **5**, 94570-47-5; **7**, 94537-47-0; **8a**, 6907-48-8; **8b**, 94537-48-1; **8c**, 94537-49-2; **9a**, 6495-83-6; **9b**, 94537-50-5; **9c**, 94537-51-6; 1,2-cyclopentanedione, 3008-40-0; 1,2-cyclohexanedione, 765-87-7; 1,2-cycloheptanedione, 3008-39-7; 1,2-cyclooctanedione, 3008-37-5; 3,4-hexanedione, 4437-51-8.

Asymmetric Synthesis. 2.[1] Practical Method for the Asymmetric Synthesis of Indolizidine Alkaloids: Total Synthesis of (-)-Monomorine I

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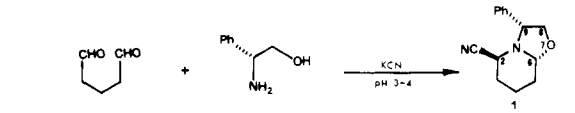
The alkylation of the chiral 2-cyano-6-oxazolopiperidine synthon (1) with the iodo ketal **2** gave, after selective cleavage of the cyano group, the oxazolopiperidine **4** having the 2*S* configuration. Compound **4** was alkylated with CH_3MgI, giving a 4:1 mixture of alcohols **6** and **7** in which the major product **6** possessed the desired 2,6-cis configuration. Treatment of **6** under acidic hydrogenation conditions (H_2, Pd/C, H^+) led to the desired (-)-monomorine I (**9**) having the 3*S*,5*R*,9*R* absolute configuration. This first asymmetric synthesis of (-)-monomorine I (**9**) establishes the absolute configuration of the natural (+)-monomorine I as 3*R*,5*S*,9*S*.

Since the isolation of monomorine I from *Monomorium pharaonis L.* by Ritter and co-workers[2] two total syntheses of the racemic form of this pharaoh ant trail pheromone[3] leading to the determination of its relative stereochemistry have been published.[4,5] More recently, a stereospecific synthesis of the racemic alkaloid **9** was reported.[6] However, no work concerning the asymmetric synthesis or the determination of the absolute configuration of monomorine I (**9**) and the related poison-dart frog gephyrotoxin 223 AB (**10b**) has appeared.[7]

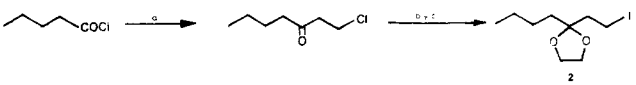
Herein we describe an enantiospecific total synthesis of (-)-monomorine I (**9**) which permitted us to assign the absolute configuration 3*R*,5*S*,9*S* to the natural (+) enantiomer.

In a recent paper[1] we reported a "one-pot" procedure for the preparation of the chiral 2-cyano-6-oxazolopiperidine synthon (**1**) from (-)-phenylglycinol, glutaraldehyde, and KCN (Scheme I). As chemo- and stereoselective reaction can be achieved at either the C-2 (α-amino nitrile) or C-6 (α-amino ether) centers of this molecule, and as hydrogenolysis produces a secondary nitrogen center capable of undergoing an intramolecular ring closure, the synthon **1** represents an ideal starting material for the chiral synthesis of the indolizidine system of **9**.

Scheme I



Scheme II



[a] Reagents: (a) $CH_2{=}CH_2$, $AlCl_3$, $CHCl_3$, 0 °C, 2 h (88% yield); (b) CH_2OHCH_2OH, PPTS, benzene, reflux, 1 h (83% yield); (c) KI, 18-crown-6, toluene, reflux, 15 h (74% yield).

Alkylation of the anion of **1** (LDA, THF, -78 °C) with iodo ketal **2** (prepared as outlined in Scheme II) led to the formation of a single product **3** isolated in 65% yield after flash chromatography on silica gel (Chart I). The amino nitrile moiety of **3** was then selectively reduced by prior complexation of the cyano group with silver ion ($AgBF_4$, THF, room temperature, 5 min) followed by reaction with $Zn(BH_4)_2$ at -50 °C (1 h). Compound **4** was obtained in 84% yield as a 3:2 mixture of C-6 epimeric oxazolidines having the 2*S* configuration.[1] A likely reversible opening of the oxazolidine ring during both the reaction workup

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